



Effectiveness of a guided self-help exercise program tailored to patients treated with total laryngectomy: Results of a multi-center randomized controlled trial



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ABSTRACT

Objective: To investigate the effectiveness of a guided self-help exercise program on swallowing, speech, and shoulder problems in patients treated with total laryngectomy (TL).

Materials and methods: This randomized controlled trial included patients treated with TL in the last 5 years. Patients were randomized into the intervention group (self-help exercise program with flexibility, range-of-motion and lymphedema exercises and self-care education program) or control group (self-care education program). Both groups completed measurements before and 3 and 6-months after randomization. The primary outcome was swallowing problems (SWAL-QOL). Secondary outcomes were speech problems (SHI), shoulder problems (SDQ), self-management (patient activation: PAM) and health-related quality of life (HRQOL: EORTC QLQ-C30/H&N35). Adherence was defined as moderate-high in case a patient exercised > 1 per day. Linear mixed model analyses were conducted to investigate the effectiveness of the intervention and to investigate whether neck dissection, treatment indication (primary/salvage TL), time since treatment, severity of problems, and preferred format (online/booklet) moderated the effectiveness.

Results: Moderate-high adherence to the exercise program was 59%. The intervention group (n = 46) reported less swallowing and communication problems over time compared to the control group (n = 46) (p-value = 0.013 and 0.004). No difference was found on speech, shoulder problems, patient activation and HRQOL. Time since treatment moderated the effectiveness on speech problems (p-value = 0.025): patients within 6 months after surgery benefitted most from the intervention. Being treated with a neck dissection, treatment indication, severity of problems and format did not moderate the effectiveness.

Conclusion: The guided self-help exercise program improves swallowing and communication.

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Introduction

Speech, swallowing and shoulder problems are often reported amongst head and neck cancer (HNC) patients treated with total laryngectomy (TL) [1–4]. A recent study amongst TL patients showed that about a quarter of all patients report unmet supportive care needs regarding problems with chewing or swallowing, difficulty speaking or problems with mobility of neck or shoulders [5].

To target these problems and needs, a self-help program has been developed for TL patients using a participatory design approach [6,7]. This self-help program called “In Tune without Cords” (ITwC) encompasses a guided self-help exercise program with exercises targeting speech, swallowing and shoulder problems and a self-care education program with information and self-care advice on speech, nutrition and mobility, as well as smelling, stoma care and voice prosthesis care. The self-care education program has previously been found to be feasible and was positively valued by TL patients in terms of general impression, ease of use, willingness to use and satisfaction with the content [7]. The guided self-help exercise program, however, has not yet been evaluated in terms of effectiveness on speech, swallowing and shoulder problems among TL patients.

Previous randomized controlled trials (RCTs) on exercise programs targeting HNC patients in general have all, except one study [8], shown beneficial effects on swallowing, speech or shoulder problems [8–19]. However, no such study specifically targeted TL patients and no study combined exercises for swallowing, speech and shoulder problems into one exercise program. The aim of this study was, therefore, to investigate the effectiveness of the guided self-help exercise program built into ITwC on swallowing, speech, and neck and shoulder problems in patients treated with TL.

Material and methods

Study design, procedure and population

This study is a prospective multi-center RCT with two treatment groups. In the intervention group patients were provided with the guided self-help exercise program and the self-care education program. In the control group, only the self-care education program was provided. Also, all patients received care as usual, which, depending on time since treatment, generally consists of allied health services as speech therapy, physiotherapy and dietary care [20]. This intervention was developed to be used in addition to care as usual, and not as replacement. Detailed information on the study is provided in the protocol paper [21]. In short, patients were asked to participate when they were treated with TL in the last five years. Patients were excluded when they were treated with TL combined with total glossectomy, were treated with a partial laryngectomy, were < 18 years, had cognitive impairments, and/or were unable to understand the Dutch language.

Patients were recruited from five different HNC centers in the Netherlands. Patients were asked to participate by their treating head and neck surgeon, speech therapist, physiotherapist or nurse specialist/practitioner at the last consultation prior to discharge, at follow-up visit or by mail plus telephone. After signing informed consent, patients were randomly assigned to either the intervention or control group. The study is registered in the Netherlands Trial Register (NTR5255) and was approved by the Medical Ethics Committee of the VU University Medical Center (2014.514) and by all participating centers on local feasibility.

Randomization

Patients were randomized into the intervention or control group by an independent person, with equal (1:1) randomization. Randomization was stratified for 1) time since TL (≤ 6 months/ > 6 months after TL); 2) neck dissection (not treated/treated with a neck dissection); and 3)

TL indication (primary/salvage TL), as these factors were hypothesized to influence the effectiveness of the intervention. Randomization was performed in blocks of two and four using an automatically created randomization list.

Self-help exercise program

The guided self-help exercise program aims to prevent or diminish swallowing, speech, and shoulder problems in TL patients. The prescribed exercises and intensity of the exercises are fixed and encompass seven flexibility exercises for the head, neck and shoulders, eight range-of-motion exercises for the tongue, lips, and jaw, and, in case of facial lymphedema, five additional lymphedema exercises. Patients randomized to the intervention group were invited by their speech therapist, physiotherapist or nurse practitioner/specialist for a consultation of half an hour during which the patient was instructed on how to perform the prescribed exercises. Following this consultation, patients were asked to perform the exercises three times a day for 12 weeks. Patients received written instructions, images and videos of the prescribed exercises, via the online application or the booklet plus DVD version. Patients could choose between these two formats. To enhance exercise adherence, patients were asked to fill in a diary during the intervention period on the performed exercises. In addition, they were coached on a weekly basis via e-mail or telephone. More information and screenshots are provided in the protocol paper [21].

Self-care education program

Patients randomized to both the intervention and control group were provided access to the self-care education program. This program provides information and self-care advice on stoma care, voice prosthesis care, speech, smelling, nutrition and mobility. Patients received the self-care education program via the online application or the booklet plus DVD version of ITwC. More information is provided in previous studies [7,21]

Study measures

Patients were asked to complete patient-reported outcome measures (PROMs) at baseline (before randomization), immediately after the intervention or control period (at approximately three months follow-up) and at six months follow-up. The primary outcome measure was swallowing problems, as measured with the swallowing quality of life questionnaire (SWAL-QOL) [22,23]. Secondary outcome measures were the speech handicap index (SHI) on speech problems in daily life [23,24], the shoulder disability questionnaire (SDQ) measuring conditions that cause pain symptoms in patients with disorders of the shoulder [25], the European Organization for Research and Treatment of Cancer generic and HNC-specific health-related quality of life (HRQOL) measures (EORTC QLQ-C30 and EORTC QLQ-H&N35) measuring cancer and HNC-specific quality of life [26,27], and the Patient Activation Measure (PAM) measuring a patient’s self-reported knowledge, skills and confidence for self-management of one’s health or chronic condition [28]. More information can be found in the protocol paper [21].

Finally, sociodemographic and clinical characteristics were measured. Sociodemographic characteristics (age, gender, education level and living situation) were measured using a study-specific questionnaire. Clinical characteristics (cancer stage, cancer treatment modality (including neck dissection), time since TL and comorbidity) were collected from the hospital information system. Comorbidity was measured using the Adult Comorbidity Evaluation 27 (ACE-27) [29].

Sample size

To demonstrate an improvement of 12 points (previously found to

be clinically meaningful [23]) on the SWAL-QOL between the intervention and control group at 6 months follow-up, using a power of 80%, a significance level of 5% and a standard deviation of 21, we aimed to include in total 100 patients (50 patients per intervention arm).

Statistical analyses

All analyses were performed using the IBM Statistical package for the Social Science (SPSS) version 22 (IBM Corp., Armonk, NY USA). First, descriptive statistics, chi-square tests and independent t-tests were performed to compare socio-demographic characteristics, clinical characteristics and PROMs at baseline between the intervention and the control group. Also, adherence to the self-help exercise program of patients randomized to the intervention group was analyzed. Adherence was defined as low in case the patient exercised, on average, ≤ 1 times a day, as moderate in case the patient exercised 1–2 time(s) a day, and as high in case the patient exercised ≥ 2 time(s) per day [30].

Linear mixed models with fixed effects for group (intervention or control) and measurement and their two-way interaction and a random effect for subject were used to compare longitudinal changes on the SWAL-QOL, SHI, SDQ, PAM, EORTC QLQ-C30 and EORTC QLQ-H&N35 in both groups over time. In addition, independent t-tests were conducted to measure differences between the intervention and control group at 3 and 6 months follow-up. Variables which were found to differ at 3 or 6 months were further examined using linear regression analyses. In the linear regression analyses we adjusted for baseline scores of the outcome variables to investigate whether the difference remained statistically significant after taking baseline differences into account.

To investigate whether being treated with a neck dissection, treatment indication (primary or salvage TL), time since treatment, severity of problems (based on the median baseline score on SWAL-QOL, SHI and SDQ) and preferred format of ITwC moderated the effectiveness, exploratory linear mixed model analyses were performed including fixed effects for time, group, their two-way interaction, the potential moderator and its two- and three-way interaction with group and time and a random intercept for subject. A significant ($p < 0.05$) three-way interaction indicates a difference of the effectiveness of the intervention group compared to the control group between groups with different scores on the investigated moderator.

All analyses were performed according to the intention-to-treat principle. A p -value < 0.05 was considered statistically significant.

Results

Study population

From June 2015 to January 2018, 253 patients were eligible and invited to participate. Of these patients, 20 patients did not provide a response or could not be reached. Of the remaining 233 patients, 92 patients (39%) were willing to participate. Of the patients whom refused participation ($n = 141$), 57 patients provided no reason for non-participation, 31 patients reported physical reasons, 12 patients reported not to be interested, 7 patients had no time and 6 patients reported psychological reasons. In addition, 28 patients had other reasons (Fig. 1).

Patients included in this study were on average 65 years old (standard deviation = 8). Most of the included patients were men (84%), lived with their partner and/or children (79%), and had an elementary or lower education level (52%) (Table 1). About a quarter of the patients were within 6 months of their TL (22%), 67% were treated with a neck dissection, and 53% were treated with salvage TL. The majority of the patients had a voice prosthesis (96%). Regarding the

ITwC format (internet or booklet), most patients favored the internet version (71%).

Of the included patients, 46 (50%) patients were randomized to the intervention group and 46 (50%) patients to the control group. There were no significant differences between the two groups in terms of socio-demographic and clinical characteristics (Table 1). Except for the sleep domain of the SWAL-QOL ($p = 0.049$), no significant differences were present at baseline on speech, swallowing and shoulder problems (Table 2). Significant baseline differences were found on HRQOL, namely all functioning domains ($p < 0.05$), and the domains on fatigue ($p < 0.001$), pain ($p < 0.001$), dyspnea ($p = 0.047$), insomnia ($p = 0.048$), loss of appetite ($p = 0.022$), constipation ($p = 0.024$) and sticky saliva ($p = 0.012$). All differences were in favor of the intervention group (i.e. better scores in the intervention group) (Table 3).

Adherence to the guided self-help exercise intervention

Of the 46 patients randomized to the intervention group, 45 patients actually started with the guided self-help exercise program, as one patient dropped out due to comorbidity before the consultation with the healthcare professional (Fig. 1). In addition, one patient died during the intervention period due to causes unrelated to the exercise program. Of the remaining 44 patients, information on adherence was available for 41 patients. Adherence was high in 20 patients (49%), moderate in 4 patients (10%), and low in 17 patients (41%).

Effectiveness of the guided self-help exercise intervention on swallowing

The course of total swallowing problems (total SWAL-QOL score) over time was significantly better in the intervention group compared to the control group (p -value two-way interaction = 0.013) (Table 2 and Fig. 2). Independent t-tests per time point showed that at 6 months follow-up patients in the intervention group had a significantly better (lower) score compared to patients in the control group (25.8 versus 34.9, $p = 0.023$). This difference remained statistically significant after adjusting for baseline scores.

The seven subdomains which together form the total SWAL-QOL score (general burden, food selection, eating duration, eating desire, fear of eating, mental health and social function) did not show a significant effect over time (p -value two-way interaction ranged from 0.055 to 0.55). Independent t-tests, however, showed significant better (lower) scores at 6 months follow-up in the intervention group compared to the control group on eating duration (45.0 versus 59.1, $p = 0.022$), fear of eating (22.9 versus 34.3, $p = 0.008$), mental health (21.4 versus 31.4, $p = 0.030$) and social function (24.9 versus 34.6, $p = 0.049$). These differences remained statistically significant after adjusting for baseline scores.

On the remaining SWAL-QOL domains (sleep, fatigue, communication and symptom score) a significant effect over time was found on the communication domain (p -value two-way interaction = 0.004). A better (lower) score in the intervention group was shown at 6 months follow-up (36.3 versus 49.9, $p = 0.015$), which remained statistically significant after correcting for baseline values.

Effectiveness of the guided self-help exercise intervention on the secondary outcomes

The course of speech problems and shoulder problems did not significantly differ over time in the intervention group compared to the control group (p -value two-way interactions were 0.57 and 0.58). Statistically significant differences on shoulder problems at 3 and 6-months follow-up were identified, however, after adjustment for baseline scores, these differences were no longer statistically significant.

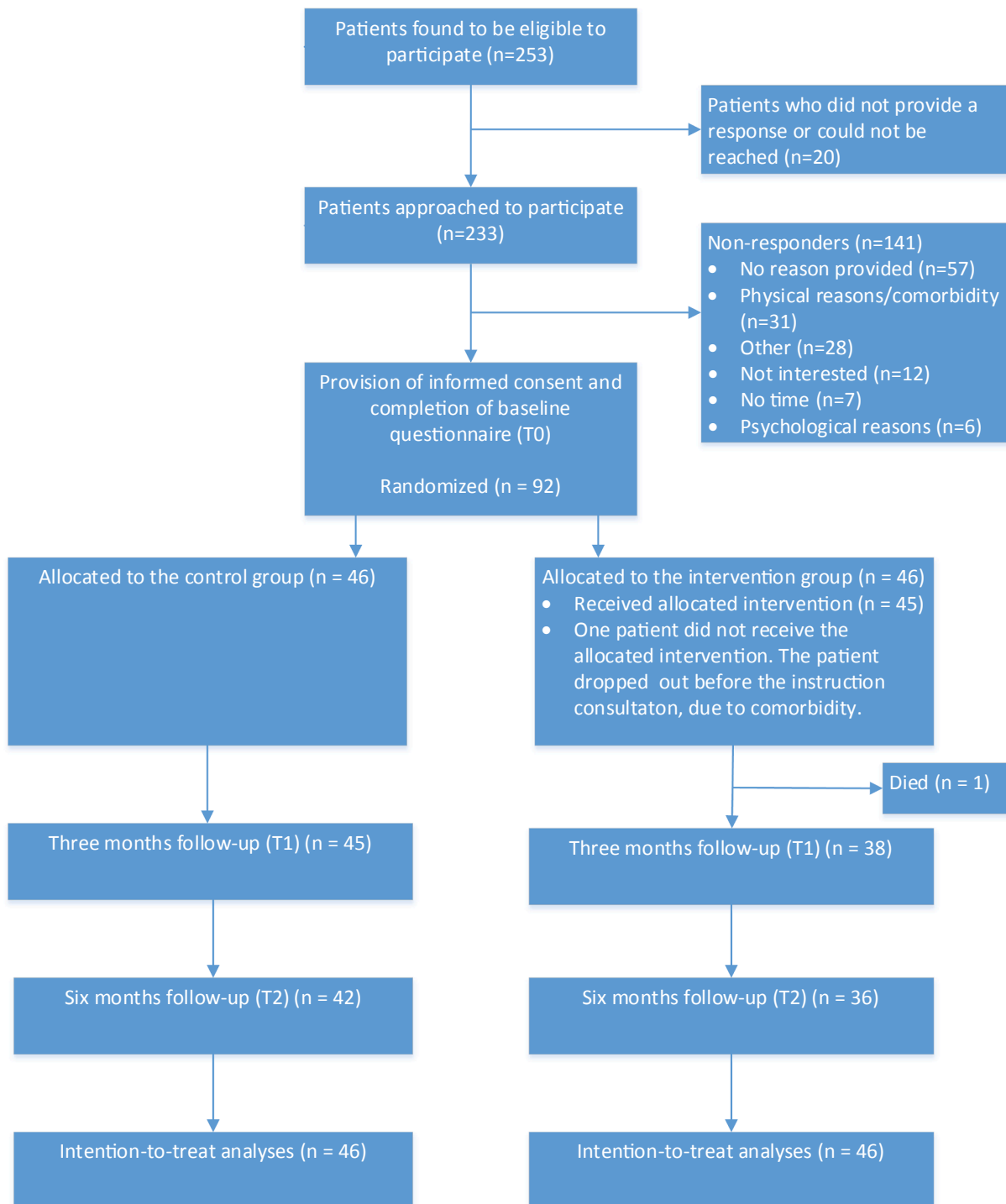


Fig. 1. Flow diagram.

Also, the course of patient activation and HRQOL (all domains) did not significantly differ between patients in the intervention and the control group (p-value two-way interactions ranged from 0.069 to 0.92) (Table 3). Some differences in HRQOL at 3 and 6-months follow-up were identified, however, after adjustment for baseline scores, these differences were not statistically significant.

Moderation analyses

Time since treatment moderated the effectiveness of the intervention on speech problems (p-value three-way interaction = 0.025) (Fig. 3). Among patients who were within 6 months after surgery, the intervention seemed to be more effective compared to control care (p-

Table 1
Baseline sociodemographic and clinical characteristics.

	Control group (n = 46)		Intervention group (n = 46)		P-value
	Number	%	Number	%	
Age (years)					
mean (SD)	64 (9)		65 (7)		0.58
Gender					0.16
men	41	89.1%	36	78.3%	
women	5	10.9%	10	21.7%	
Living situation¹					0.20
living alone	7	15.6%	12	26.7%	
living together (with partner and/or children)	38	84.4%	33	73.3%	
Education level¹					0.41
elementary	5	11.1%	4	8.9%	
lower	22	48.9%	16	35.6%	
secondary	7	15.6%	13	28.9%	
higher	11	24.4%	12	26.7%	
Employment status					0.36
employed in paid work	5	10.9%	10	21.7%	
not employed or not able to work	17	37.0%	14	30.4%	
retired	24	52.2%	22	47.8%	
Time since total laryngectomy (months)					
Mean (SD)	19 (15)		24 (18)		0.11
< 6 months	10	21.7%	10	21.7%	1.00
6 months - 5 years	36	78.3%	36	78.3%	
Type of total laryngectomy					1.00
primary	21	45.7%	22	47.8%	
salvage	25	54.3%	24	52.2%	
Treated with a neck dissection					1.00
yes	31	67.4%	31	67.4%	
no	15	32.6%	15	32.6%	
Surgery prior to total laryngectomy					0.40
yes	9	19.6%	6	13.0%	
no	37	80.4%	40	87.0%	
Treatment with (chemo)radiation before or after total laryngectomy					0.56
yes	38	82.6%	40	87.0%	
no	8	17.4%	6	13.0%	
Comorbidity²					0.64
none	11	23.9%	13	26.4%	
mild	25	54.3%	20	44.4%	
moderate/severe	10	21.7%	12	26.7%	
Current speech method (multiple answers possible)³					
voice prosthesis	45	97.8%	42	93.3%	0.36
injection method ⁴	1	2.2%	1	2.2%	NA
electrolarynx ⁴	2	4.3%	0	0%	NA
other (e.g. cannot speak) ³	0	0%	3	6.5%	NA
Preferred format⁵					0.14
booklet and DVD	16	36.4%	10	22.2%	
internet	28	63.6%	35	77.8%	

Abbreviations: NA, not assessed due to small number. ¹ Missing in two patients. ² Missing in one patient. ³ Missing in two patients. ⁴ Differences between the two groups were not statistically assessed, because of low number of patients who scored positive on these questions. ⁵ Missing in three patients.

value two-way interaction = 0.038), while for patients who were treated longer than 6 months ago the intervention was as effective as control care (p-value two-way interaction = 0.91). No evidence was found for a moderating effect of time since treatment on the effectiveness of the intervention on swallowing and shoulder problems (p-value three-way interaction = 0.083 and 0.93). Also, no evidence was found that treatment indication (primary or salvage TL), being treated with a neck dissection (on shoulder problems), severity of problems at baseline as measured using the SWAL-QOL, SHI and SDQ and preferred ITwC format moderated the effectiveness of the intervention (all p-value three-way interaction > 0.10).

Discussion

This study aimed to investigate the effectiveness of a guided self-help exercise program on swallowing, speech, and neck and shoulder problems in patients treated with TL. Results showed that patients in the intervention group reported less swallowing problems over time, compared to the control group. Also, less communication problems

were reported over time in the intervention group compared to the control group. No main differences between the two groups were reported on speech problems, shoulder problems, patient activation and HRQOL.

Our finding that the guided self-help exercise program improves swallowing problems is in line with previous RCTs, except for one [8], which all showed beneficial effects of (prophylactic) exercises, device-based exercises (Therabite) or a combination of both on swallowing-related outcomes among HNC patients [9,10,14,15,18,19]. Our study adds to these previous studies by providing evidence for the effectiveness of a guided self-help exercise program which combines flexibility and range-of-motion exercises for swallowing, speech and shoulder problems. Strengthening exercises were not provided as part of this intervention, although recognized for their importance in rehabilitation care, because we only aimed to include easy to perform exercises for which patients only have to come to the medical center once for instructions.

We found that this guided self-help exercise program was effective in improving the total SWAL-QOL score over time compared to the

Table 2
Results linear mixed model analyses and independent t-test analyses of speech, swallowing and shoulder problems.

Outcome	Group	Linear mixed model analyses			Independent t-tests								
		Course over time			Baseline		T1 (3 months follow-up)		T2 (6 months follow-up)				
		n	F (df) two-way interaction ¹	p-value two-way interaction	n	mean	SD	n	mean	SD	n	mean	SD
SWAL-QOL													
Total score	Control	46			46	32.7	16.3	44	31.4	17.6	42	35.0	17.9*
	Intervention	46	4.494 (155.79)	0.013*	45	29.2	16.9	37	28.4	16.2	36	25.8	17.1
General burden	Control	46			46	37.7	26.1	44	35.3	23.9	42	38.8	26.9
	Intervention	46	0.608 (159.53)	0.55	45	32.6	23.0	37	32.2	23.9	36	30.7	27.0
Food selection	Control	46			46	24.8	22.4	44	23.9	23.4	42	28.1	26.6
	Intervention	46	1.127 (156.03)	0.33	45	24.8	26.0	37	25.2	19.0	36	23.7	18.1
Eating duration	Control	46			46	54.8	24.0	44	57.1	22.5	42	59.1	21.7*
	Intervention	46	2.957 (156.72)	0.055	45	48.6	25.0	37	48.8	27.5	36	45.0	29.9
Eating desire	Control	46			46	27.9	18.2	44	28.8	18.6	42	29.4	19.3
	Intervention	46	1.074 (156.96)	0.34	45	28.3	16.9	37	28.8	17.8	36	24.5	19.4
Fear of eating	Control	46			46	32.0	18.1	44	30.0	21.9	42	34.3	17.5**
	Intervention	46	2.525 (157.13)	0.083	45	28.7	21.6	37	25.7	19.7	36	22.9	19.4
Mental health	Control	46			46	28.6	21.9	44	26.6	22.8	42	31.4	21.2*
	Intervention	46	2.667 (155.25)	0.073	45	25.2	18.7	37	23.9	18.3	36	21.4	18.6
Social function	Control	46			46	32.4	23.6	44	30.2	24.7	42	34.6	23.5*
	Intervention	46	2.530 (155.03)	0.083	45	27.3	21.7	37	26.6	17.7	36	24.9	19.0
Sleep	Control	46			46	45.8	26.0*	44	45.6	30.4 ²	42	46.6	31.2
	Intervention	46	0.029 (156.64)	0.97	46	35.6	23.0	37	32.3	25.1	36	33.1	23.6
Fatigue	Control	46			45	46.8	23.1	44	45.1	23.0	42	43.5	21.8 ²
	Intervention	46	0.352 (155.45)	0.70	46	38.4	21.9	37	38.1	17.8	36	33.2	19.9
Communication	Control	46			46	45.8	26.3	44	49.9	23.5*	42	49.2	24.7
	Intervention	45	5.812 (154.54)	0.004**	44	47.3	26.5	37	36.3	25.5	35	39.7	29.1
Symptom score	Control	46			46	34.3	14.9	44	32.1	14.3	42	33.0	15.0
	Intervention	46	0.122 (157.24)	0.89	46	28.8	16.3	37	28.3	12.0	36	29.6	17.2
SHI													
Total score	Control	45			39	43.1	19.8	38	45.9	23.1	37	44.9	22.7
	Intervention	42	0.571 (129.50)	0.57	40	39.0	20.7	35	36.9	19.0	31	37.5	24.1
Psychosocial functioning	Control	46			42	18.5	11.8	39	17.9	12.2	40	18.0	11.7
	Intervention	44	0.602 (139.68)	0.55	42	16.2	11.2	36	14.1	9.9	34	14.5	11.4
Speech functioning	Control	45			41	24.1	9.0	41	25.4	10.4	38	25.4	10.0
	Intervention	43	0.513 (139.48)	0.60	42	22.2	9.7	36	21.2	9.3	33	20.9	11.8
SDQ													
Total score	Control	46			45	36.9	38.0	43	37.0	38.2 ²	42	37.6	38.2 ²
	Intervention	46	0.551 (156.489)	0.58	46	24.2	34.0	37	21.1	32.4	35	18.6	32.5

*Indicates a p-value below 0.05. ** indicates a p-value below 0.01 and *** indicates a p-value below 0.001. ¹Numerator df = 2. ²This differences were no longer statistically significant after adjusting for baseline score.

control group. In addition, significant effects on eating duration, fear of eating, mental health and social function (subscales of the SWAL-QOL) between the two groups were shown at medium-term follow-up. The finding that beneficial results on swallowing are present, even after the intervention period ended, are in line with the previous study of Kotz et al. [10] which showed sustainable effects of prophylactic exercises on swallowing up to 6 months after the intervention among HNC patients treated with chemoradiation. Surprisingly, we found, no effect on swallowing as measured using the swallowing domain of the EORTC QLQ-H&N35. This might, however, be due to the fact that the SWAL-QOL has more items on swallowing and therefore can better detect small differences between groups than the EORTC QLQ-H&N35.

Besides swallowing problems, we also found a beneficial effect of the guided self-help program on the course of communication, as measured using the corresponding subscale of the SWAL-QOL. This finding was remarkable, as no significant main effect was found on the secondary outcome measure on speech problems (SHI). Moderation analyses did, however, show beneficial effects on the SHI among a small group of patients within 6 months after TL surgery. A previous study that focused on the effectiveness of a program with exercises targeting voice among HNC patients during or after cancer treatment also showed positive pre- to post intervention improvements [31]. These findings indicate that an exercise program as ITwC may be especially effective on speech outcomes in the first phase of the rehabilitation process.

Finally, no significant effect of the guided self-help intervention was

found on shoulder problems, self-management and HRQOL. The lack of a significant effect on shoulder problems is in contrast to previous RCTs, which showed that other exercise programs, such as a progressive resistance exercise program, is effective on shoulder-related outcomes in HNC patients treated with a neck dissection [11,13,17]. To investigate whether our self-help exercise program is effective among TL patients treated with a neck dissection specifically, we performed a sub-analyses on the moderating effect of being treated with a neck dissection. These results, however, confirmed our finding that the guided self-help program was not effective in improving shoulder. An explanation for this lack of effectiveness may be the used measurement instrument (SDQ), which mainly measures pain instead of mobility of the shoulder.

A reason why this study did not show significant differences on self-management and HRQOL may be that both groups were provided with the self-care education program encompassing information and self-care advice on stoma care, voice prosthesis care, speech, smelling, nutrition and mobility. Also, all patients received care as usual, which often consists of speech therapy, physiotherapy and/or dietary care [20]. In addition, the adherence rate was, although in line with other exercise programs [30,32], relatively low (i.e. 59%). We aimed to improve adherence in this study by contacting patients via telephone or e-mail on a weekly basis to motivate them to perform the exercises and by asking them to complete a diary on the number of times practiced each day. However, further attention should be paid on improving adherence, for example by adding behavioral component techniques as

Table 3
Results linear mixed model analyses and independent t-test analyses of patient activation and health-related quality of life.

Outcome	Group	Linear mixed model analyses			Independent t-tests								
		Course over time			Baseline			T1 (3 months follow-up)			T2 (6 months follow-up)		
		n	F (df) two-way interaction ¹	p-value two-way interaction	n	mean	SD	n	mean	SD	n	mean	SD
PAM													
Total score	Control	46			43	59.3	15.9	43	58.7	16.6	40	61.9	16.5
	Intervention	44	0.187 (148.84)	0.83	42	60.4	15.9	33	59.1	12.9	35	64.5	20.1
EORTC QLQ-C30													
Global quality of life	Control	46			45	71.9	19.7	44	71.8	20.4	42	72.6	18.6
	Intervention	46	0.305 (153.186)	0.74	45	77.4	17.7	37	76.6	22.0	33	80.6	15.3
Physical functioning	Control	46			45	73.5	21.5**	44	76.6	18.9**	42	77.1	19.8*
	Intervention	46	0.554 (156.011)	0.58	46	84.2	15.6	37	87.0	13.6	36	85.9	17.4
Role functioning	Control	46			45	65.6	34.2**	44	71.6	29.1**	42	75.8	25.6
	Intervention	46	2.404 (153.900)	0.094	46	85.5	21.8	37	87.8	21.0	35	83.8	21.6
Emotional functioning	Control	46			45	72.0	24.3**	44	77.7	21.3	42	76.4	21.1*
	Intervention	46	1.532 (156.228)	0.22	46	85.3	19.2	37	85.1	22.1	36	87.0	17.6
Cognitive functioning	Control	46			45	80.4	18.6**	44	82.6	19.3*	42	86.9	16.7
	Intervention	46	2.716 (158.079)	0.069	46	91.7	13.5	37	91.0	12.8	36	90.7	16.6
Social functioning	Control	46			45	71.1	24.2*	44	76.5	21.4	42	76.2	24.2
	Intervention	46	1.404 (155.704)	0.25	46	81.9	21.0	37	82.4	22.2	36	84.7	21.2
Fatigue	Control	46			45	38.4	27.5**	44	32.8	26.9*	42	32.3	25.7*
	Intervention	46	1.649 (155.851)	0.20	46	21.0	22.9	37	20.3	19.5	36	20.1	22.8
Nausea Vomiting	Control	46			45	5.6	11.8	44	7.6	18.8*	42	6.3	16.4
	Intervention	46	0.917 (158.697)	0.40	46	2.9	6.4	37	0.9	3.8	36	3.2	11.8
Pain	Control	46			45	27.8	33.1**	44	27.7	30.3*	42	24.2	26.6*
	Intervention	46	0.793 (157.005)	0.45	46	12.7	17.3	37	13.1	19.7	36	12.0	20.9
Dyspnea	Control	46			44	35.6	29.1*	44	31.8	28.7	42	28.6	29.1
	Intervention	46	0.696 (156.610)	0.50	46	23.9	26.0	37	25.2	28.8	36	18.5	25.8
Insomnia	Control	46			45	29.6	30.3*	44	28.8	32.6	42	26.2	34.2
	Intervention	46	0.645 (157.729)	0.53	46	18.1	24.0	36	15.7	24.5	36	18.5	24.5
Loss of appetite	Control	46			45	14.1	21.9*	44	11.4	22.7	42	12.7	24.4
	Intervention	46	1.753 (156.076)	0.18	46	5.1	14.0	37	7.2	16.0	36	8.3	20.1
Constipation	Control	46			45	12.6	23.9*	44	9.8	21.1	42	15.9	25.8*
	Intervention	46	1.871 (163.401)	0.16	46	3.6	10.5	37	6.3	17.3	36	4.6	11.7
Diarrhea	Control	46			44	8.3	20.5	44	5.3	12.3	41	4.9	11.9
	Intervention	46	2.657 (152.999)	0.073	46	5.8	17.6	37	4.5	17.9	36	8.3	21.6
Financial problems	Control	46			45	25.9	35.5	44	26.5	32.6	42	23.0	33.3
	Intervention	46	0.285 (157.661)	0.75	46	13.8	21.7	37	15.3	30.0	35	16.2	26.0
EORTC QLQ-H&N35													
Oral pain	Control	46			45	11.5	15.3	44	9.7	13.4	42	6.5	12.8
	Intervention	46	1.241 (156.260)	0.29	45	9.3	14.6	37	6.3	9.3	36	7.9	12.9
Swallowing	Control	46			45	15.7	15.2	44	12.1	15.2	42	16.6	22.5
	Intervention	46	0.901 (160.525)	0.41	45	13.5	15.8	37	14.6	16.6	36	14.6	20.1
Senses problems	Control	46			45	47.8	25.5	44	49.6	27.7	42	54.4	29.0
	Intervention	46	2.683 (157.481)	0.071	45	45.6	27.4	37	44.1	27.6	36	43.0	32.5
Speech problems	Control	46			46	33.7	23.8	44	29.8	26.1	42	26.5	24.9
	Intervention	44	0.160 (157.387)	0.85	44	27.5	21.5	36	21.8	21.2	35	21.1	23.3
Trouble with social eating	Control	46			45	18.5	24.0	44	14.4	21.1	42	17.5	25.4
	Intervention	46	0.323 (156.946)	0.72	46	13.9	18.0	37	12.6	15.2	36	15.9	22.3
Trouble with social contact	Control	46			46	17.4	19.5	44	13.4	15.5	42	12.1	14.7
	Intervention	46	0.522 (156.298)	0.59	46	11.7	17.1	36	9.3	17.0	36	9.6	16.5
Sexuality	Control	46			43	35.3	31.3	42	33.7	36.5	39	36.8	37.7
	Intervention	46	0.569 (142.510)	0.57	45	37.4	38.5	33	26.8	31.7	33	27.8	34.8
Teeth	Control	46			45	17.0	28.1	44	11.4	18.9	42	9.5	21.2
	Intervention	46	2.506 (157.250)	0.085	45	12.6	22.8	37	12.6	19.8	36	13.9	20.1
Opening mouth	Control	46			45	18.5	28.0	44	15.2	25.4	42	17.5	27.8
	Intervention	46	0.220 (156.586)	0.80	45	14.1	25.1	37	11.7	22.5	36	13.9	28.0
Dry mouth	Control	46			45	10.4	17.1	43	7.8	16.0	42	11.9	21.9
	Intervention	46	0.736 (155.875)	0.48	45	8.1	14.5	37	9.9	19.0	36	9.3	18.9
Sticky saliva	Control	46			45	31.1	32.1*	44	29.5	33.1*	42	33.3	32.9**
	Intervention	46	0.376 (156.891)	0.69	44	15.9	23.3	37	14.4	20.1	36	13.9	21.6
Coughing	Control	46			45	35.6	29.6	44	31.8	28.7	42	32.5	34.1
	Intervention	46	0.140 (157.987)	0.87	45	36.3	29.1	37	33.3	26.1	36	31.5	26.4
Felt ill	Control	46			45	14.8	20.8	44	14.4	24.3	42	16.7	22.4
	Intervention	46	0.079 (158.566)	0.92	45	9.6	18.3	37	9.0	16.9	36	11.1	19.5

*Indicates a p-value below 0.05. ** indicates a p-value below 0.01 and *** indicates a p-value below 0.001. ¹Numerator df = 2. After adjustment for baseline scores, all of the differences at 3 and 6 months follow-up were no longer statistically significant.

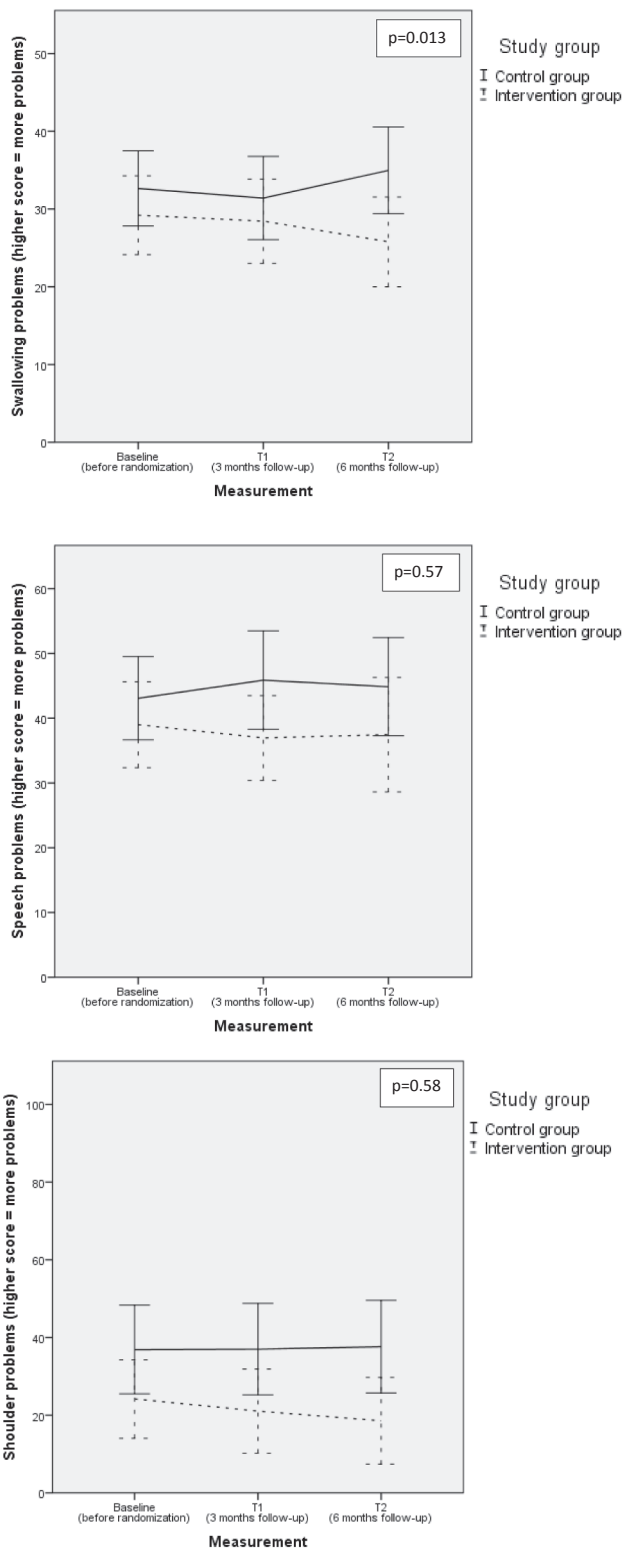


Fig. 2. The course of swallowing, speech and shoulder problems in the intervention and control group.

monitoring of the outcome by the patient [33,34]. Such techniques may be easily built into the online version of such interventions. Results of our study showed that the effectiveness of the online version of the application is comparable to that of the booklet version and that the majority of the patients preferred the online format. This supports, as

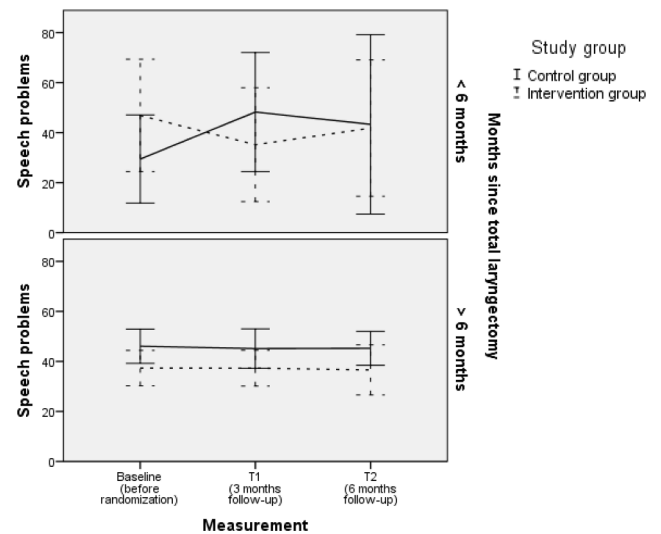


Fig. 3. Moderation by time since total laryngectomy. Time since treatment moderated the effectiveness of the intervention group compared to the control group on speech problems (p-value three-way interaction is 0.025). Separate linear mixed model analyses per group (< 6 months and > 6 months) showed p-values of the two-way interaction of 0.038 (< 6 months) and 0.91 (> 6 months).

also hypothesized in previous studies [7,35], the feasibility of online programs for this patient group.

Another way to improve adherence to this intervention may be by further tailoring this guided self-help exercise program to the individual patient. We asked all patients to perform all exercises targeting swallowing, speech, and shoulder problems, as we aimed to both diminish and prevent these problems. Since preventing these problems may be most relevant for patients during or shortly after treatment, we did investigate whether time since treatment moderated the effectiveness of the intervention. These analyses showed that time since treatment moderated the effectiveness on speech but not on shoulder or swallowing problems. Further insight is needed into which specific exercises are beneficial for which group of patients.

A limitation of this study is that we did not reach the a priori defined sample size of 100 patients. Recruitment of patients was difficult, as TL is only performed about 150 times a year in the Netherlands [36] and not all centers performing TL participated in our study. We managed to include 92 patients which was, as our standard deviation found was lower than expected a priori, nevertheless sufficient to demonstrate an improvement of 12 points using a power of 92% and a significance level of 5%. Another limitation of this study was the low response rate of 39%, which may have resulted in selection bias. In addition, participants in the intervention group scored significantly better at baseline, however, we adjusted for these differences in the analyses. Nevertheless, this might have limited the possibility to find effects on HRQOL. Finally, we used the SWALQOL and SHI to measure swallowing problems and speech problems, as these measures have been validated among Dutch TL patients [23], however laryngectomy-specific questionnaires [37,38] or objective measurements may have added important information.

In conclusion, our study showed that the guided self-help exercise program improves swallowing and communication among TL patients. More insight is, however, needed into opportunities to tailor the program to the individual patient and to improve adherence to the exercises.

Declaration of Competing Interest

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Appendix A. Supplementary material

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